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Cerebrovascular Response to Step-Wise Increase in Inspired Oxygen Tension From Control (Air) to 100% Oxygen.

Nine experiments have been performed on 9 normal human volunteer subjects, utilizing a control period and step-wise increases in inspired oxygen concentration (and hence tension). It was originally shown by S. S. Kety and his colleagues, utilizing the nitrous oxide method for cerebral blood flow, together with arterial-venous oxygen difference across the brain, that inspired oxygen in 85 to 100% concentration does not affect the oxygen consumption of the brain. Under these circumstances, the reciprocal of the arterial-venous oxygen difference across the brain will, as the Fick equation indicates, vary as the cerebral blood flow. In the present experiments, arterial and internal jugular venous samples were drawn at constant rate during the last 15 seconds of each 10-minute period and carried over into the first 15 seconds of the next 10-minute period. These were analyzed for oxygen content in the Van Slyke gas analysis apparatus, and the reciprocal of the arterial-venous oxygen difference calculated from these data.

The results indicated no statistically significant change in the mean cerebral blood flow at any level of oxygenation, although with 100% oxygen there was a small (approximately 7%) reduction in mean cerebral blood flow.

These studies are somewhat at variance with those reported by Kety and Schmidt (J. Clin., Invest. 27:484, 1948), in which 85 - 100% $O_2$ produced a reduction in cerebral blood flow from a mean of 52 to a mean of 45 cc/100gm/brain/min. It is to be noted that in the Kety and Schmidt experiments the 100% oxygen was administered for from 15 to 30 minutes before the subject was switched to 85% $O_2$ - 15% $N_2O$ for the measurement of cerebral blood flow and oxygen consumption. The procedure then required 10 additional minutes of the inhalation of oxygen in high concentration. It should be noted, however, that the mean arterial-internal jugular venous oxygen difference in the control period in these 6 subjects of Kety and Schmidt was 6.2 vols. percent and in the experimental period the $^1/(A\text{-}V)_{O_2}$ was 7.1 vols. percent. Since there was no significant change in cerebral oxygen consumption (3.1 vs. 3.2 cc/100gm/min), the cerebral blood flow decreased by the same amount as calculated by either the $N_2O$ or the $^1/(A\text{-}V)_{O_2}$ method, namely 13 percent.

One may interpret our data as indicating that a form of adaptation occurs when small graded increments of inspired oxygen, and hence of arterial oxygen, are produced for 10 minute periods. It appears doubtful that the random errors in the method can account for the absence of significant changes in cerebral blood flow, as measured by the $^1/(A\text{-}V)_{O_2}$ method, to hypoxia in the graded increments indicated above. This adaptive response on the part of the blood vessels, or perhaps blood vessels and brain, has implications of considerable physiologic interest as well as practical importance.

Cerebrovascular Responses to Hyperoxia Induced by Abrupt Change From Air to 100% Inspired Oxygen.

The study reported below indicated different responses when the inspired gas mixture was abruptly changed from 21% oxygen i.e. air to 100% oxygen. The methods employed were similar to those described above. In six studies on five normal subjects, the cerebral blood flow was measured at successive 10 minute intervals after the subjects were shifted from air to oxygen breathing. End-tidal carbon dioxide tension was monitored with the infra-red $CO_2$ analyzer to provide an approximate measure of alveolar $CO_2$ tension, and therefore of arterial $CO_2$ tension, which was maintained at control values during the oxygen breathing by voluntary adjustment of ventilation. Actually, minimal mean of fall in arterial $CO_2$ tension occurred, amounting to approximately 2 mm Hg. Previous studies from this laboratory have shown that this change in arterial $CO_2$ tension would not account for the vasoconstriction observed, since this degree of decrease below control represents the approximate threshhold change in $PaCO_2$ required to initiate any cerebral vasoconstriction.

The results are summarized in the accompanying chart which carries the same title as the heading to this section. It can be seen that within 20 minutes or less the major reduction in cerebral blood flow had occurred, amounting to an approximately 17% decrease below control level. This change was statistically significant. It will be noted that after 50 minutes a small further reduction in cerebral blood flow had occurred, the total change at this point amounting to an almost 20% reduction below the control blood flow level. The possibility of fatigue of the vaso-constrictor response after this point is raised by the fact that between the 50 and 60 minute samples, in 5 of the 6 studies, a slight increase in

cerebral blood flow occurred, although the actual flow value remained significantly below the control level.

It is probable that more prolonged studies, perhaps lasting as long as 90 minutes (if the volunteer subject would tolerate it) would be required to evaluate the question of "fatigue" of the vasoconstrictor response to 100% oxygen inhalation and its accompanying arterial oxygen tension of approximately 600 mm Hg.

Studies Using In Vitro Systems of the Response of a Thermistor Blood Velocity Needle Probe

A needle type of flowmeter inserted into the superior bulb of the internal, jugular vein of man would have great advantages in the study of both normal and abnormal states of cerebral blood flow. One of the major advantages is complete continuity of data. Previously we have had a thermistor needle probe constructed for us by subcontract from Lexington Instruments, Waltham, Mass. Two of these needle probes were promising, but had excessive instability. An initial study has been made of a new probe's (High Temperature Instruments Corp., Philadelphia) response characteristics to changes in velocity of fluid flow in a polyethylene tube into which the probe was inserted. Measurements were made on a cathode oscilloscope recorder of the response of the flow probe during changes in velocity of streamline flow within the tube. The response of the probe in these experiments has been found to be logarithmic in a system in which the velocity of flow ranged from 60 mm per minutes to 352 per minute, at a fluid temperature of 37° C (See attached figure). The fact that the probe's response to flow changes is logarithmic in form, fits the prediction of Dr. Alex Clarke, Biophysics Department, Medical College of Virginia. If heat dissipation is assumed to be linearly related to velocity of flow, Dr. Clarke's analysis, using the manufacturer's data on resistances for various temperatures predicts that the relationship between change in velocity of flow and the resistence would be logarithmic, as was found.

Pilot work has been done on calibrating the probe for given environmental temperatures by switching from the probe to a heliopot resistor in a bridge circuit to determine the resistence of the probe at any given temperature. Thus, a series of resistence values plotted against tempera ture will allow the probe to be used initially to measure temperature of

the fluid environment. Further determinations of this type are needed to show reproducibility of resistence values for the probe under similar conditions. Finally the probe must be calibrated for a given flow at a given temperature. These determinations will be done using the constant temperature water bath which was used for the previously discussed determinations of flow. Following these calibrations the probe will be tested in dogs to measure the flow rate in the jugular bulb of these animals. The probe will be inserted into the jugular bulb and an initial determination will be made of the resistence of the probe by using the heliopot resistor as before. By using the previous calibrations together with the resistence of the probe the initial temperature of the jugular bulb can be determined. Then, by turning on the probe heater, velocity of blood will be measured by comparing the flow in the dog for a given initial jugular blood temperature to the calibration flows for the same initial temperature.

A final decision regarding the relative advantages of thermistor vs thermocouple type probes for this application has not been made. We have had difficulty with stability and reproducability of thermistor performance on repetitive calibration runs. Thermocouples, on the other hand, require much greater amplification of the signal. No commercially available probe has been found which meets all of our design requirements.

## BIBLIOGRAPHY


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ABSTRACTS

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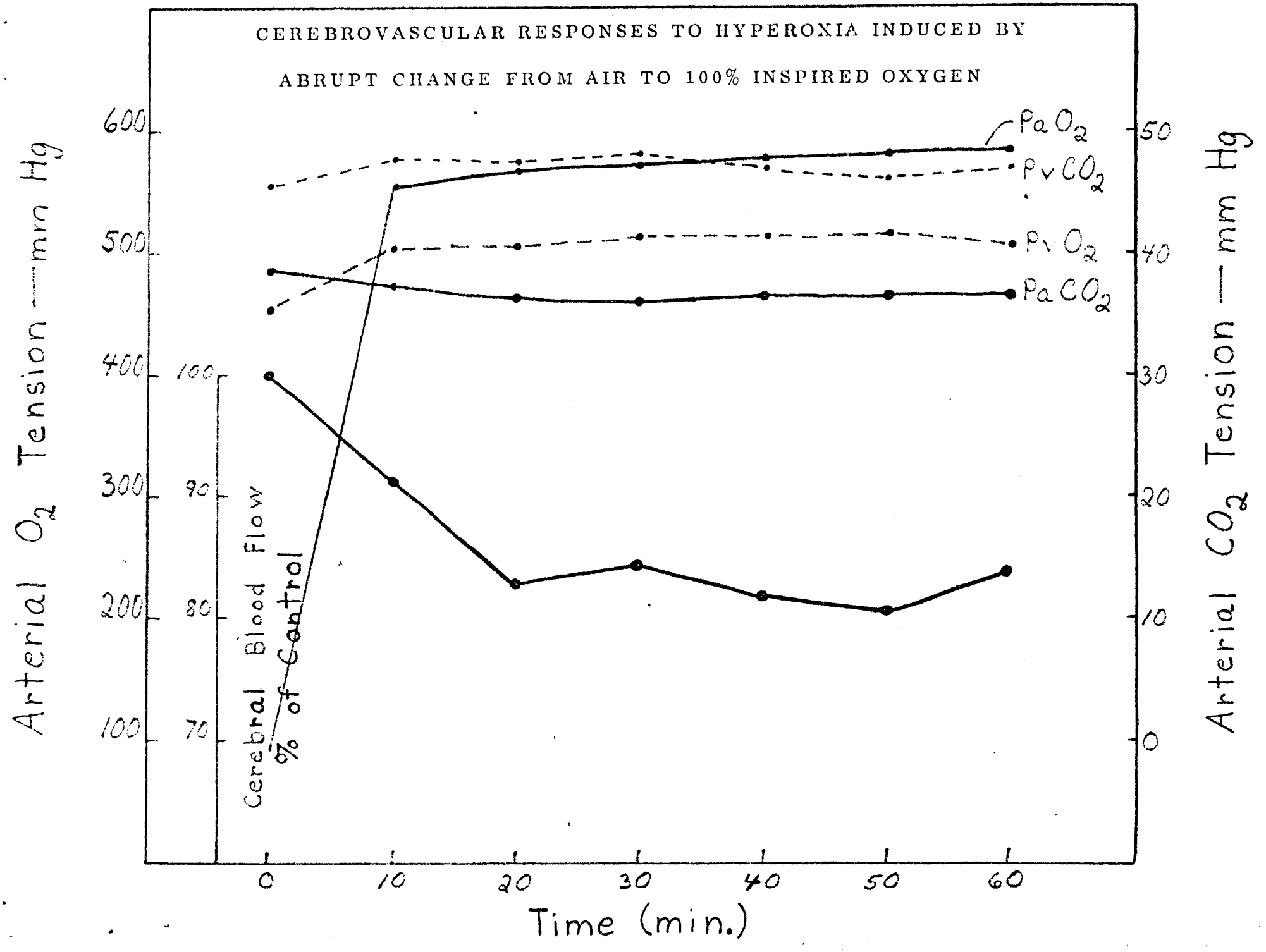
CEREBROVASCULAR RESPONSES TO HYPEROXIA INDUCED BY
ABRUPT CHANGE FROM AIR TO 100% INSPIRED OXYGEN
Arterial $O_2$ Tension — mm Hg
Arterial $CO_2$ Tension — mm Hg
$Pa O_2$
$P\bar{v} CO_2$
$P\bar{v} O_2$
$Pa CO_2$
Cerebral Blood Flow % of Control
Time (min.)
600
500
400
300
200
100
50
40
30
20
10
0
100
90
80
70
0
10
20
30
40
50
60

# Calibration Curve of Thermal Needle Probe